

Surgical Indication and Approach are Associated with Transfusion in Hysterectomy for Benign Disease

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ABSTRACT

Objective: To identify pre-operative and intraoperative factors associated with the risk of red blood cell transfusion among women undergoing hysterectomy.

Methods: A retrospective cohort study of hysterectomy for benign indications between January 1, 2011 – December 31, 2017. Patients receiving blood transfusion within 30 days of surgery were compared to patients who did not receive any transfusion. Multivariate logistic regression analysis was performed to identify clinical and surgical variables associated with blood transfusion.

Results: Among 171,940 women who underwent hysterectomy for benign indication, 4,667 (2.7%) required blood transfusion. The rate of transfusion was highest among patients with uterine fibroids (4.3%) and lowest in patients with genital prolapse (1.1%) ($p < 0.05$). Odds of blood transfusion were significantly elevated in patients undergoing hysterectomy for uterine fibroids compared to patients with genital prolapse (adjusted odds ratio [aOR] 1.36, 95% confidence interval [CI] 1.15 – 1.61). Other patient

characteristics included body mass index, smoking, bleeding disorders, pre-operative sepsis, and American Society of Anesthesiologists score ≥ 2 ($p < 0.05$). Higher pre-operative hematocrit significantly decreased the risk of blood transfusion (aOR 0.84, 95% CI 0.84 – 0.85 per percent increase in hematocrit). Abdominal and vaginal hysterectomies were associated with greater odds of transfusion compared with laparoscopic approaches (aOR 5.06, 95% CI 4.70 – 5.44; aOR 1.87, 95% CI 1.67 – 2.10, respectively).

Conclusion(s): Certain patient comorbidities, surgical indication, and approach to hysterectomy are associated with increased risk of blood transfusion. These results may have implications for pre-operative patient counseling, perioperative care, and health system planning.

Key Words: Blood transfusion, Hysterectomy, Laparoscopy, Uterine diseases.

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INTRODUCTION

Hemorrhage requiring blood transfusion is a serious complication of hysterectomy. There are several potential adverse events associated with transfusion, ranging from allergic reaction and febrile nonhemolytic transfusion reaction to serious events with long-term sequelae, such as hemolysis, infection transmission, and iron overload.¹ Besides the major effect on overall morbidity and mortality, blood transfusion has a significant impact on the health care system with chronic shortage of blood products in blood banks.^{2,3}

Bleeding outcomes vary with surgical factors including approach to hysterectomy, where greater estimated blood loss and rates of blood transfusion have been reported in patients undergoing abdominal hysterectomy as compared to laparoscopic and vaginal approaches.⁴⁻⁶ Additionally, while rates of transfusion of hysterectomies performed for benign indications is 2.6%,⁵ the rate is lower for hysterectomies performed using a minimally invasive approach at 1.3%.⁷ Other risks factors identified from large cohort studies include age, nonwhite race, American Society of Anesthesiolo-

gists (ASA) class, bleeding disorders, pre-operative hematocrit, and platelet count. However, these studies included hysterectomies performed for both benign and malignant conditions as well as myomectomies, which are known to carry different levels of risk.^{5,7–10} Furthermore, the use of multivariable analysis to control for potential confounders has not been used in several of these studies,^{7,9} making it difficult to appreciate the individual effects of each variable.

Among other potential risk factors, various uterine diseases likely confer different levels of bleeding risk. Menstrual disorders and uterine fibroids are conditions characterized by heavy menstrual bleeding, which may predispose patients to requiring blood transfusions. Furthermore, the type of uterine disease has been shown to be an important determinant of other surgical outcomes, including surgical site infection and venous thromboembolism.^{11,12} While the association between surgical indication and risk of transfusion has been inferred using other measures including uterine weight and pre-operative anemia, no study has specifically assessed pelvic disease as an independent risk factor. Understanding the relationship between surgical indication and transfusion risk can assist surgeons and patients in adequately assessing and preparing for surgical complications and improve quality of care. We hypothesize that the need for blood transfusion in women undergoing hysterectomy would be associated with surgical indications of menstrual disorders and uterine fibroids due to blood loss associated with the disease process, as well as abdominal surgical approaches, which are more invasive and often reserved for more complex cases.

We conducted a large retrospective cohort study to investigate the pre-operative and intraoperative risk factors for blood transfusion among women undergoing hysterectomy for benign indications.

MATERIALS AND METHODS

This study was reviewed and approved by the Institutional Review Board. A retrospective cohort analysis using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database was performed. Women who underwent hysterectomy for benign indications from January 1, 2011 – December 31, 2017 were identified using Current Procedural Terminology (CPT) codes (58150, 58152, 58180, 58260, 58262-3, 58267, 58270, 58275, 58280, 58290-4, 58541-4, 58550, 58552-4, 58570-3). Indication for hysterectomy was classified according to the International Statistical Classification of Diseases and Rel-

ated Health Problems (ICD-9 and ICD-10) codes into fibroids (ICD-9 218; ICD-10 D25), menstrual disorders (ICD-9 6260.2–6260.9, 6270.0; ICD-10 N92, N93), genital prolapse (ICD-9 618; ICD-10 N81), endometriosis (ICD-9 617; ICD-10 N80), pain (ICD-9 6250.0–6250.3, 6250.5, 6250.7; ICD-10 N94), and other. We excluded patients with malignant disease, patients undergoing emergency (nonelective) surgery, and patients who had other surgical procedure(s) within 30 days prior to hysterectomy.

Baseline patient characteristics included age, race, body mass index (BMI), smoking status, presence of comorbid conditions (diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, hypertension requiring medication, and bleeding disorder), and ASA classification status. BMI was classified according to the World Health Organization classification system into Under-weight (< 18.5), Normal (18.5 – 24.9), Overweight/Pre-obesity (25.0 – 29.9), Obesity Class I (30.0 – 34.9), Obesity Class II (35.0 – 39.9), and Obesity Class III (≥ 40). Perioperative characteristics included route of surgery (abdominal, vaginal, or laparoscopic), total or subtotal hysterectomy, and operative time. Robotic-assisted laparoscopic surgery was included as laparoscopic surgery. Blood transfusion is defined in the NSQIP database as having received whole or packed red blood cells within 72 hours of surgery start time.

Patients who received blood transfusion were compared with patients who did not receive blood transfusion, in terms of patient baseline and process-of-care variables. Mean values and standard deviations (SD) were calculated for age and BMI. Proportion of blood transfusion was calculated for all categorical variables. In the bivariate analyses, categorical variables were compared using χ^2 tests and odds ratios (OR) with 95% confidence intervals (CI) calculated for each category. Patient characteristics, indication for surgery, and perioperative variables that were significant on univariate analysis or considered to be clinically relevant were included in the multivariate logistic regression model, and adjusted odds ratios (aOR) with 95% CI were calculated. Two-sided p-values < 0.05 were considered statistically significant. For variables with multiple categories (i.e., surgical indication, surgical approach), categories with the lowest proportion of transfusion were selected as the referent category in the regression analysis. All analyses were carried out using SAS version 90.3. (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 171,940 women who underwent hysterectomy for benign indications in the ACS-NSQIP database during

the study period were included in the analysis. Uterine fibroids were the most common indication for hysterectomy (33.5%), followed by menstrual disorders (21.4%), genital prolapse (12.4%), endometriosis (7.0%), and pelvic pain (3.6%).

Overall, 2.7% of patients required blood transfusion following hysterectomy. Pre-operative characteristics with higher rates of blood transfusion were ages 40 – 49 years, nonwhite race, extremes of BMI, additional comorbidities (diabetes mellitus, hypertension, congestive heart failure, bleeding disorders), lower pre-operative hematocrit, pre-operative sepsis, and higher ASA classification ($P < .05$). Rates of transfusion were also higher in patients with uterine fibroids, who underwent abdominal compared with laparoscopic or vaginal hysterectomy, and who had subtotal compared with total hysterectomy ($P < .05$). Rates of transfusion decreased with increasing year of operation ($P < .05$, **Table 1**).

Following adjustment for potential confounders, odds of blood transfusion was highest among women undergoing hysterectomy for uterine fibroids compared to women undergoing hysterectomy for genital prolapse (aOR 1.36; 95% CI 1.15 – 1.61). Compared with blood transfusion rates for abdominal hysterectomy (7.2%), blood transfusion rates for laparoscopic and vaginal hysterectomy were similarly low (1.2%; 1.8%, respectively) (**Table 1**). On multivariate analysis, abdominal and vaginal hysterectomies had higher odds of transfusion compared with laparoscopic hysterectomy (aOR 5.06; 95% CI 4.70 – 5.44, aOR 1.87; 95% CI 1.67 – 2.10, respectively; **Table 2**).

Other patient factors associated with red blood cell transfusion included younger age, BMI < 18.5, nonwhite race, bleeding disorders, pre-operative sepsis, and ASA ≥ 2 ($P < .05$, **Table 2**). For every increase in hematocrit by 1%, the odds of transfusion decreased by 16% (aOR 0.84, 95% CI 0.84 – 0.85) (**Table 2**).

DISCUSSION

Hemorrhage requiring blood transfusion is a serious complication of hysterectomy and is associated with many adverse sequelae including wound complications, thromboembolic events, and sepsis.⁷ Given that hysterectomies are one of the most common surgeries performed in women,¹³ it is important to understand the underlying factors that increase risk of bleeding and transfusion to improve quality of care. In this retrospective cohort study of 171,940 women undergoing hysterectomy for benign indication, the overall rate of blood transfusion was 2.7%,

consistent with current literature,⁵ with the highest rates of transfusion in patients presenting with uterine fibroids and menstrual disorders. Several pre-operative and surgical characteristics were associated with increased odds of transfusion, including age, weight, race, hematologic abnormalities, and baseline health status and approach to hysterectomy.

Women undergoing hysterectomy for uterine fibroids and menstrual disorders experienced the highest rates of transfusion, likely given patients with these conditions present with heavy menstrual bleeding and lower pre-operative hemoglobin. When adjusted for other clinical and surgical variables including hematologic parameters uterine fibroids were associated with greater odds of transfusion compared with other indications. In addition, Black race – which has been shown to be a risk factor for fibroids, increased severity of symptoms, and increased rates of hospitalization for fibroids – was also independently associated with blood transfusions.^{14,15}

While fibroids are known to increase risk of transfusion, to our knowledge, this is the first study to quantify the risk of fibroids on perioperative blood transfusion compared to other surgical indications. Uterine fibroids may predispose patients to bleeding and blood transfusions through several mechanisms. First, fibroids are thought to increase vascularity and blood flow to the uterus, which may be a source of iatrogenic bleeding complications.¹⁶ Second, hysterectomies for uterine fibroids are often complex and challenging due to the distortion of normal pelvic anatomy caused by the presence of fibroids. Third, as surgical complexity is a key consideration in choice of surgical approach, larger fibroids may require an open abdominal approach, which was also shown to be independently associated with transfusion in our study.

Though patients with uterine fibroids may have increased propensity to adverse bleeding outcomes, hematologic variables were associated with perioperative blood transfusion, including lower pre-operative hematocrit and bleeding disorders at baseline.^{10,17} Women with bleeding disorders have additional complexities, as they are more likely to present with heavy menstrual bleeding, which in turn constitutes their indication for hysterectomy.¹⁸ Importantly, pre-operative anemia has also been shown to increase mortality rate,¹⁹ and interestingly, the risk of postoperative adverse events associated with pre-operative anemia does not appear to be corrected by perioperative transfusion.⁸ Together, these findings highlight the importance of decreasing menstrual blood flow and

Table 1.

Baseline Characteristics of Women Undergoing Hysterectomy for Benign Indications With and Without Blood Transfusion, American College of Surgeons National Surgical Quality Improvement Program, 2011 – 2017

Variable	Total	Blood Transfusion		p-value
		Yes, n (%)	No, n (%)	
Blood transfusion	171,940	4,667 (2.7)	167,273 (97.3)	n/a
Age (years)				< 0.01
< 40	35,046	907 (2.6)	34,139 (97.4)	
40 – 44	36,627	1,236 (3.4)	35,391 (96.6)	
45 – 49	39,847	1,261 (3.2)	38,586 (96.8)	
50 – 54	24,194	691 (2.9)	23,503 (97.1)	
55+	36,226	572 (1.6)	35,654 (98.4)	
Race				< 0.01
White	132,162	2,472 (1.9)	129,690 (98.1)	
Black	30,169	1,678 (5.6)	28,491 (94.4)	
Other	9,609	517 (5.4)	9,092 (94.6)	
BMI				< 0.01
Underweight	1,347	56 (4.2)	1,291 (95.8)	
Normal	38,539	925 (2.4)	37,614 (97.6)	
Overweight	49,525	1,283 (2.6)	48,242 (97.4)	
Obese I (BMI < 35)	38,373	984 (2.6)	37,389 (97.4)	
Obese II (BMI 35 – 40)	23,054	652 (2.8)	22,402 (97.2)	
Obese III (BMI ≥ 40)	21,102	767 (3.6)	20,335 (96.4)	
Smoking	29,477	701 (2.4)	28,776 (97.6)	< 0.01
COPD	1,799	43 (2.4)	1,756 (97.6)	0.40
Diabetes	13,759	450 (3.3)	13,309 (96.7)	< 0.01
Hypertension	48,144	1,415 (2.9)	46,729 (97.1)	< 0.01
Congestive heart failure	128	8 (6.3)	120 (93.8)	0.01
Bleeding disorder	1,486	128 (8.6)	1,358 (91.4)	< 0.01
Chronic steroid use	2,637	72 (2.7)	2,565 (97.3)	0.96
Pre-operative Sepsis	481	55 (11.4)	426 (88.6)	< 0.01
Pre-operative Hematocrit [n, Mean (SD)]	171,940	4,667, 33.46 (5.91)	167,273, 38.87 (4.05)	< 0.01
Pre-operative platelet count [n, mean (SD)]	171,940	4,667, 313.39 (108.32)	167,273, 275.85 (72.78)	< 0.01
ASA class				< 0.01
ASA 1	18,133	356 (2)	17,777 (98)	
ASA 2	116,417	2,878 (2.5)	113,539 (97.5)	
ASA 3-4-5	37,390	1,433 (3.8)	35,957 (96.2)	
Year of surgery				< 0.01
2011	11,163	370 (3.3)	10,793 (96.7)	
2012	15,712	453 (2.9)	15,259 (97.1)	
2013	20,883	613 (2.9)	20,270 (97.1)	
2014	24,938	742 (3.0)	24,196 (97.0)	

Table 1. Continued

Variable	Total	Blood Transfusion		p-value
		Yes, n (%)	No, n (%)	
2015	29,370	811 (2.8)	28,559 (97.2)	
2016	34,695	858 (2.5)	33,837 (97.5)	
2017	35,179	820 (2.3)	34,359 (97.7)	
Return to OR	4,667	493 (10.6)	4,174 (89.4)	< 0.01
Indication for hysterectomy				< 0.01
Endometriosis	12,002	253 (2.1)	11,749 (97.9)	
Genital prolapse	21,362	241 (1.1)	21,121 (98.9)	
Menstrual disorders	36,757	866 (2.4)	35,891 (97.6)	
Uterine fibroids	57,528	2,484 (4.3)	55,044 (95.7)	
Pelvic pain	6,121	77 (1.3)	6,044 (98.7)	
Other	38,170	746 (1.9)	37,424 (98.1)	
Surgical approach				< 0.01
Abdominal	40,671	2,946 (7.2)	37,725 (92.8)	
Laparoscopic	102,473	1,202 (1.2)	101,271 (98.8)	
Vaginal	28,796	519 (1.8)	28,277 (98.2)	
Total				< 0.01
Total	154,581	4,100 (2.7)	150,481 (97.4)	
Subtotal	17,359	567 (3.3)	16,792 (96.7)	
Uterine weight				< 0.01
< 250g	111,318	1,183 (1.1)	110,135 (98.9)	
> 250g	19,616	529 (2.7)	19,087 (97.3)	

ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease. Data are n (%) unless otherwise specified.

supplementing iron stores to optimization of hematologic parameters prior to surgery.

The ASA classification system is a method for anesthesiologists to assess pre-operative risk in patients undergoing surgery. In this study, we found ASA is also associated with increased odds of perioperative transfusion. As the ASA classification takes any patient comorbidity into consideration, it is difficult to determine which of these comorbidities specifically contributes to increased risk of transfusion. However, patients with additional comorbidities may have less physiologic reserve to tolerate bleeding and low hemoglobin. These findings may also reflect recommendations for a higher hemoglobin threshold for certain patient populations, including those with pre-existing cardiovascular disease.²⁰

Among other pre-operative characteristics, we found lower BMI was associated with increased risk of blood transfusion. The literature to date suggests higher BMIs do not have

higher rates of transfusions compared to normal BMI;^{21–25} however, there is limited evidence comparing underweight women to normal BMI. In other surgical populations, patients in higher weight categories demonstrate higher pre-operative blood volumes and less perioperative blood loss per kilogram of their weight, which in turn is associated with decreased transfusion requirements.^{26,27} At a biochemical level, obesity is associated with a procoagulant state, with increased procoagulant enzymes, inhibitors of fibrinolysis, and platelet aggregation, which may contribute to decreased blood loss.^{28–30} Interestingly, in pelvic reconstructive surgery and other surgical procedures, obesity has been associated with decreased rates of adverse surgical outcomes, including risk of transfusion,^{26,31} suggesting improvements in bariatric surgical techniques.

Surgical approach is a key factor in operative blood loss. Abdominal approach to hysterectomy was associated with

Table 2.

Effect of Patient and Process-of-care Characteristics on Blood Transfusion Among Women Undergoing Hysterectomy for Benign Indication, American College of Surgeons National Surgical Quality Improvement Program, 2011 – 2017

Variable	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio* 95% CI
Age (years)		
< 40	Referent	Referent
40 – 44	1.32 (1.21 – 1.43)	0.98 (0.89 – 1.08)
45 – 49	1.23 (1.13 – 1.34)	0.86 (0.78 – 0.94)
50 – 54	1.11 (1.00 – 1.22)	0.93 (0.83 – 1.03)
55+	0.60 (0.54 – 0.67)	0.85 (0.74 – 0.96)
BMI		
Underweight	1.76 (1.34 – 2.32)	1.52 (1.12 – 2.06)
Normal	Referent	Referent
Overweight	1.08 (0.99 – 1.18)	0.97 (0.89 – 1.06)
Obese I (BMI < 35)	1.07 (0.98 – 1.17)	0.85 (0.77 – 0.94)
Obese II (BMI 35 – 40)	1.18 (1.07 – 1.31)	0.85 (0.76 – 0.95)
Obese III (BMI ≥ 40)	1.53 (1.39 – 1.69)	0.96 (0.85 – 1.07)
Race		
White	Referent	Referent
Black	3.09 (2.90 – 3.29)	1.26 (1.17 – 1.36)
Other	2.98 (2.71 – 3.29)	2.03 (1.82 – 2.25)
Comorbidities		
Smoking	0.85 (0.78 – 0.92)	0.87 (0.80 – 0.95)
Diabetes	1.24 (1.12 – 1.36)	0.99 (0.88 – 1.11)
Hypertension	1.12 (1.05 – 1.20)	0.95 (0.88 – 1.03)
Congestive heart failure	2.4 (1.17 – 4.91)	1.01 (0.46 – 2.22)
Pre-operative sepsis	4.67 (3.52 – 6.20)	2.50 (1.80 – 3.48)
Hematologic variables		
Bleeding disorder	3.45 (2.87 – 4.14)	2.84 (2.31 – 3.50)
Pre-operative Hematocrit	0.82 (0.81 – 0.82)	0.84 (0.84 – 0.85)
Pre-operative platelet count	1.00 (1.00–1.01)	1.00 (1.00 – 1.00)
ASA class		
ASA I	Referent	Referent
ASA 2	1.27 (1.13 – 1.42)	1.21 (1.07 – 1.36)
ASA 3–4-5	1.99 (1.77 – 2.24)	1.79 (1.56 – 2.05)
Surgical indication		
Endometriosis	1.89 (1.58 – 2.25)	1.22 (0.99 – 1.49)
Genital prolapse	Referent	Referent
Menstrual disorders	2.11 (1.83 – 2.44)	1.15 (0.97 – 1.37)
Uterine fibroids	3.95 (3.46 – 4.52)	1.36 (1.15 – 1.61)
Pain	1.12 (0.86 – 1.44)	0.93 (0.70 – 1.23)
Other	1.75 (1.51 – 2.02)	1.10 (0.93 – 1.31)

Table 2. Continued

Variable	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio* 95% CI
Surgical approach		
Abdominal	6.58 (6.15 – 7.04)	5.06 (4.70 – 5.44)
Laparoscopic	Referent	Referent
Vaginal	1.55 (1.39 – 1.72)	1.87 (1.67 – 2.10)
Total vs. Subtotal	0.81 (0.74 – 0.88)	1.06 (0.96 – 1.17)

CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists.

*Adjusted for age, body mass index, race, pre-operative comorbidities, hematologic variables, ASA classification, surgical indication, surgical route, and total/subtotal hysterectomy.

the highest odds of transfusion. This has been well documented in the literature, with abdominal approaches carrying significantly higher risk of bleeding and subsequent blood transfusion.^{5,32} Though vaginal and laparoscopic approaches were previously found to be comparable in outcomes,³³ we found laparoscopic approaches decreased odds of blood transfusion compared to vaginal hysterectomy with regards to blood transfusions. While these results may partly reflect patient selection, this association was observed even following adjustment for patient and disease factors.³⁴

The strengths of this study include the use of the NSQIP database, which is a large multi-institutional database, allowing for the generalizability of these results. Given that patients within the database are consistently followed for 30 days following surgery, there is a reduced risk of confounding due to differences in length of stay or loss-to-follow-up. In addition, the large amount of clinical and surgical variables collected in the database allowed for multivariate regression modelling to control for potential confounding effects. To our knowledge, this study is the first to evaluate the association of surgical indication for hysterectomy with respect to the risk of blood transfusion.

Limitations of this investigation include the lack of detailed clinical information regarding the type and severity of pelvic disease and details regarding pre-operative preparation, which can impact surgical outcomes. For example, hematocrit rather than hemoglobin was available for analysis within the NSQIP database, and this is reflected in our results. The NSQIP database also relies on voluntary participation of institutions, which may result in self-selection bias. Additionally, despite the rigor with which Surgical Clinical Reviewers are trained to perform chart abstraction and data entry in a standardized fashion, the potential for missing information and coding errors exists.

CONCLUSION

This study identified pre-operative and intraoperative factors, particularly surgical indication and approach, that are independently associated with increased risk of blood transfusion in women undergoing hysterectomy. The identification of these factors may be useful for improved pre-operative risk assessment and multidisciplinary optimization for elective surgery to reduce the need for transfusion perioperatively.

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